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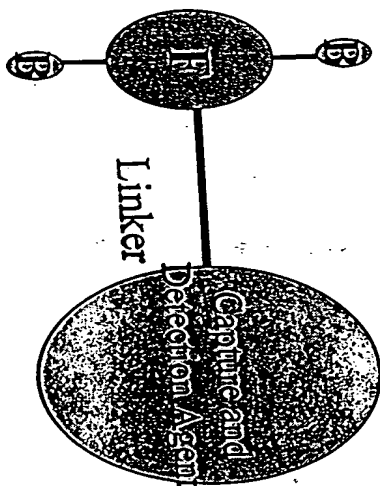
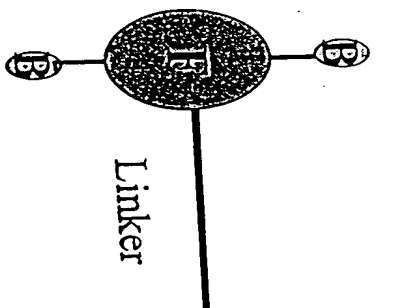
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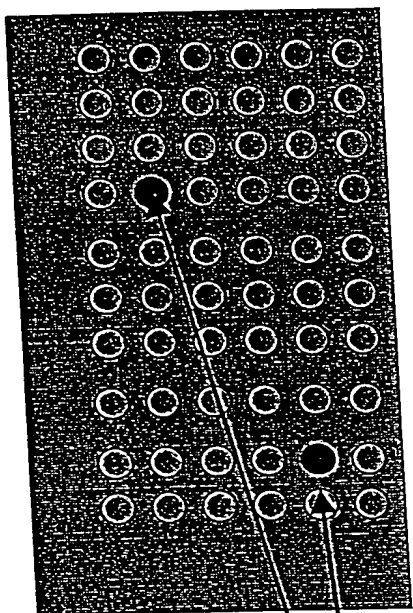
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High-throughput Target ID



Library of Bioactive
Compounds

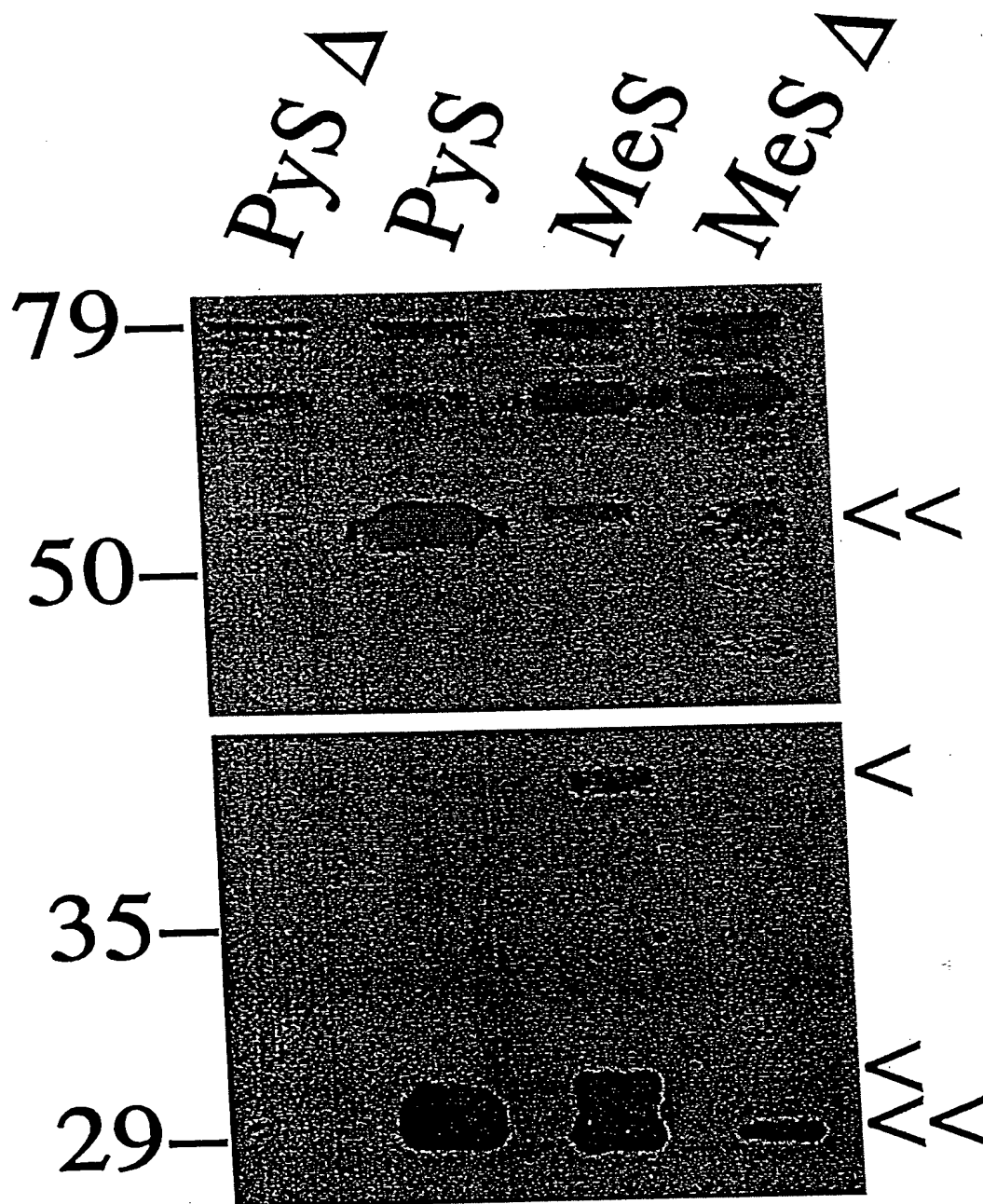


Library of Target ID
Compounds

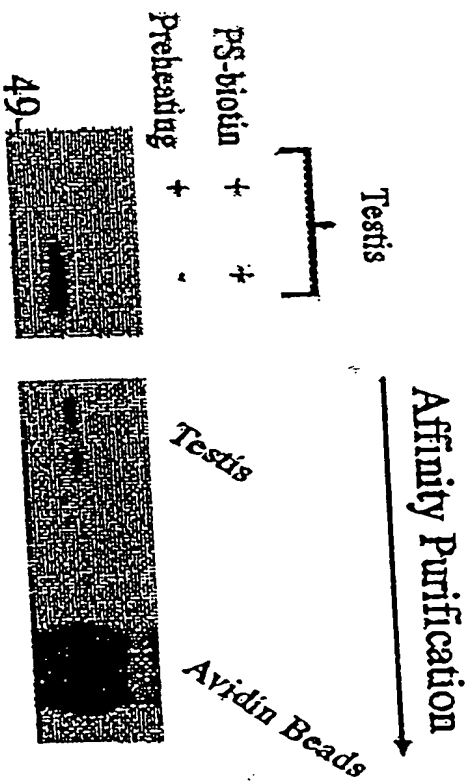
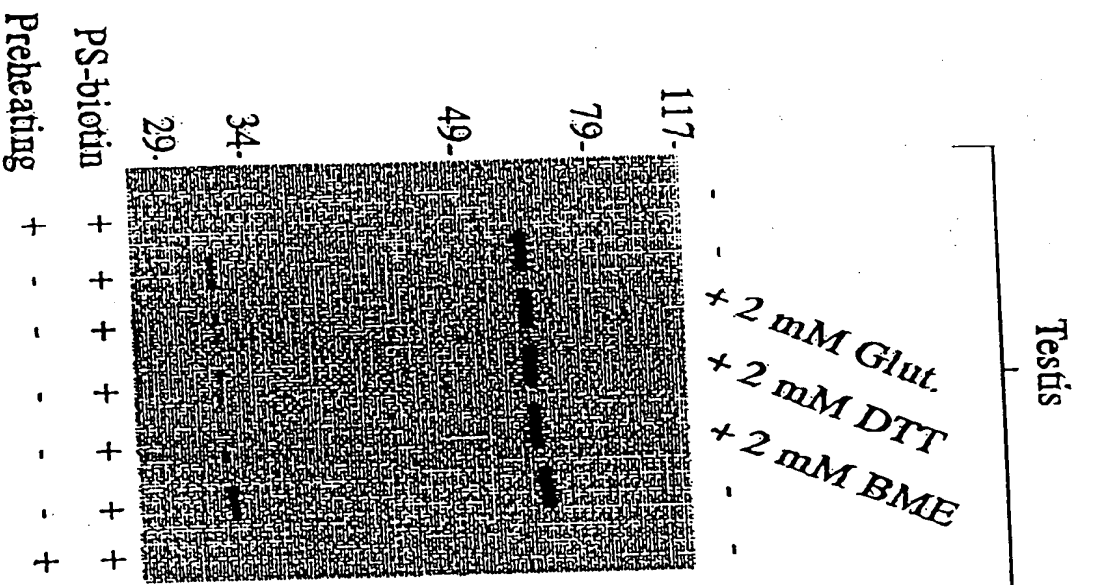
Use corresponding
activity-based probe to
identify the biological target

FIGURE 1

FIGURE 2



Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes

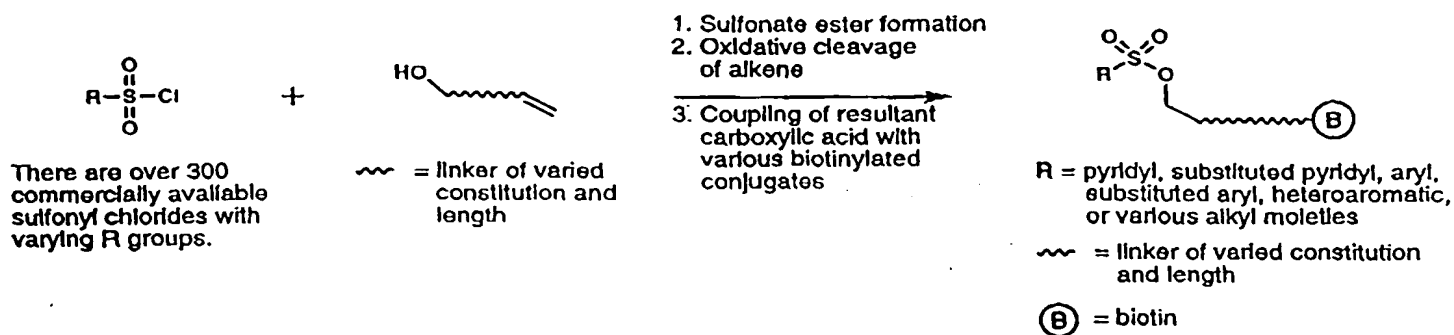


- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)

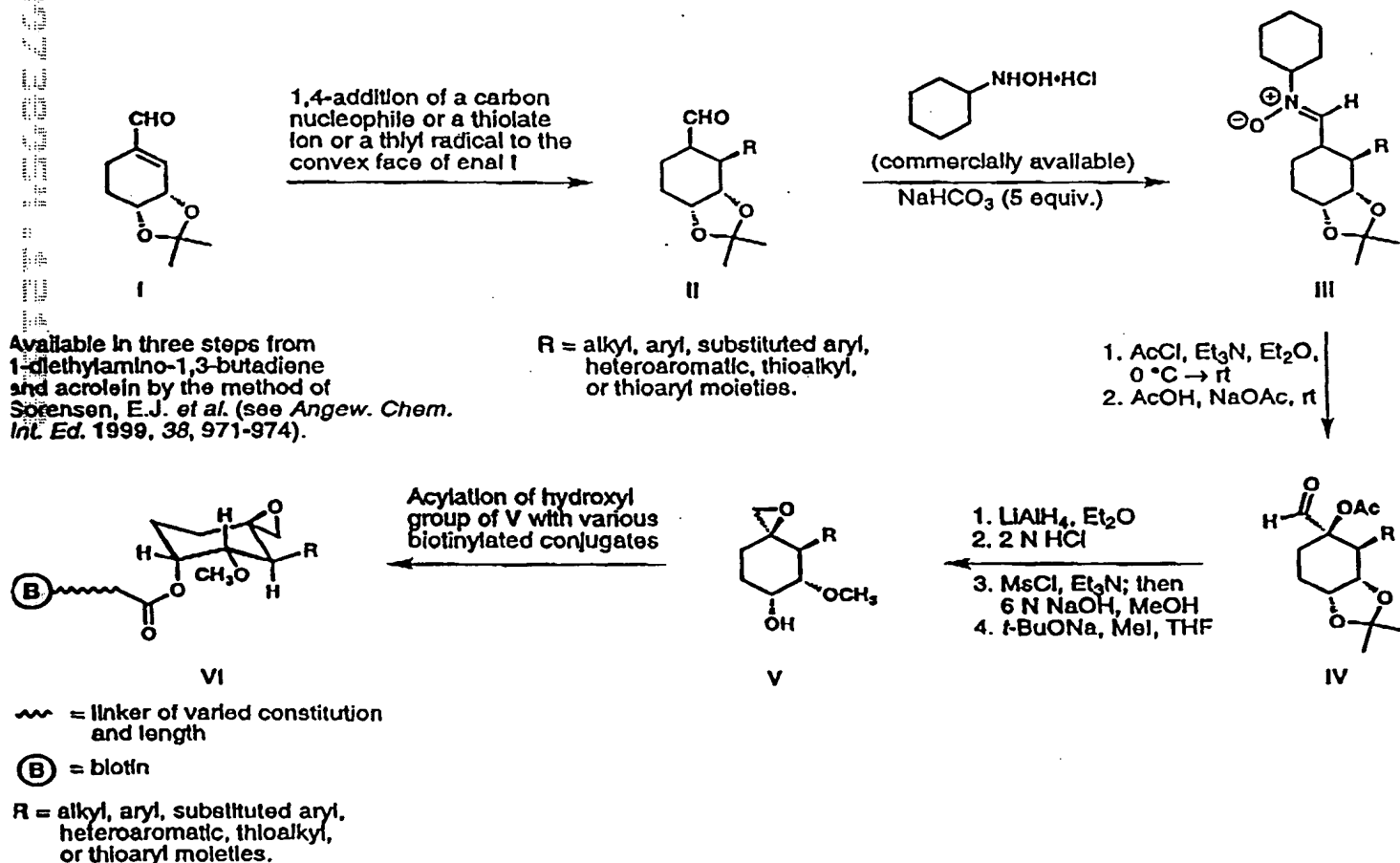
- 28 ADHs in fly genome
 - Involved in retinoic acid biosynthesis and catabolism of alcohol and chemotherapeutic agents

FIGURE 3

FIGURE 4



Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



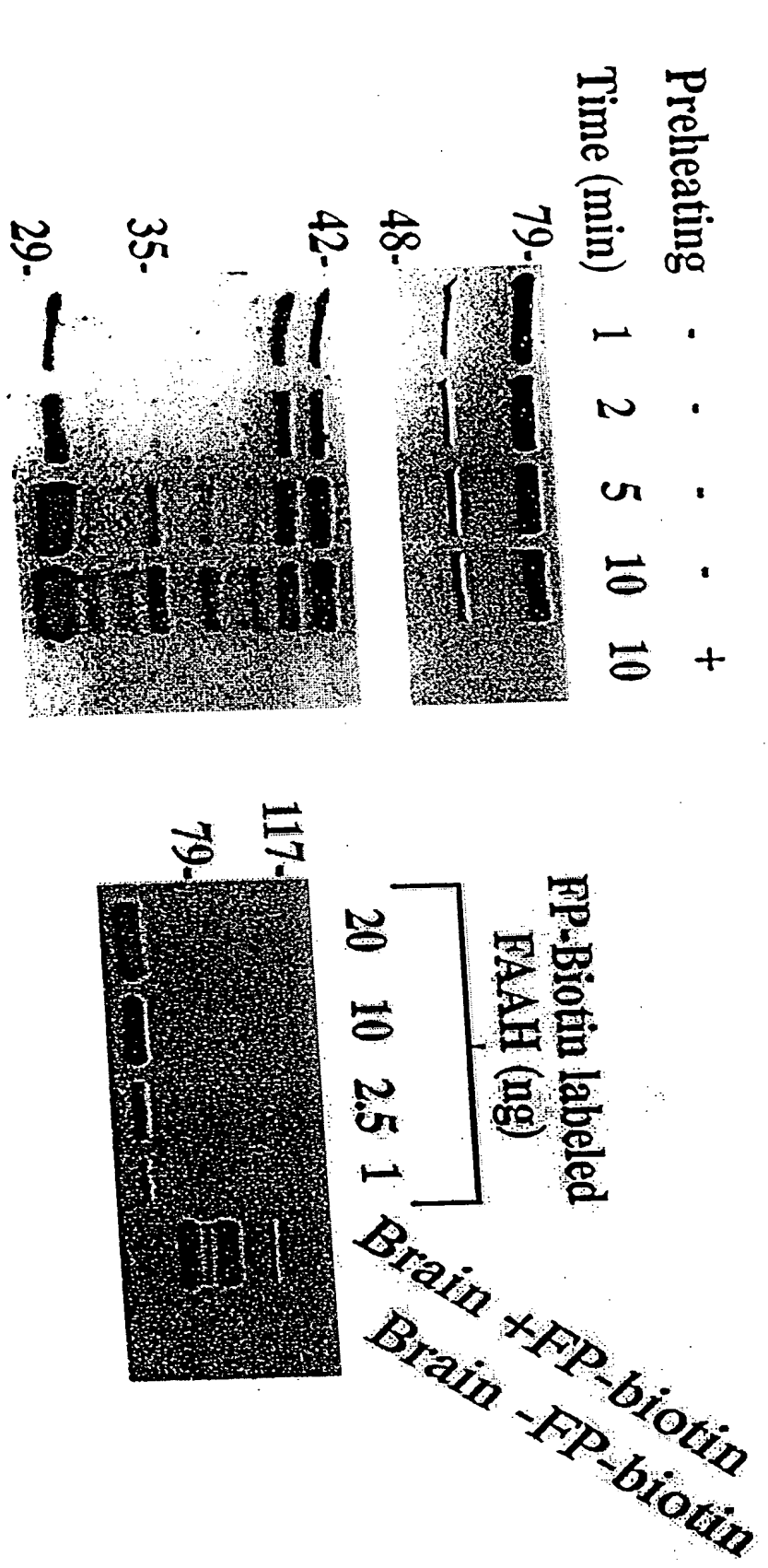
Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for $\text{I} \rightarrow \text{II} \rightarrow \text{III} \rightarrow \text{IV} \rightarrow \text{V}$ can be found in Sorensen, E.J. *et al.* *Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

FP-Biotin: a kinetic reporter of SH Activity

The rates at which the majority of SHs react with FP-biotin can be experimentally followed

FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes

FIGURE 5



Utility of Multiplexed probes in identifying Serine Hydrolases

FIGURE 6

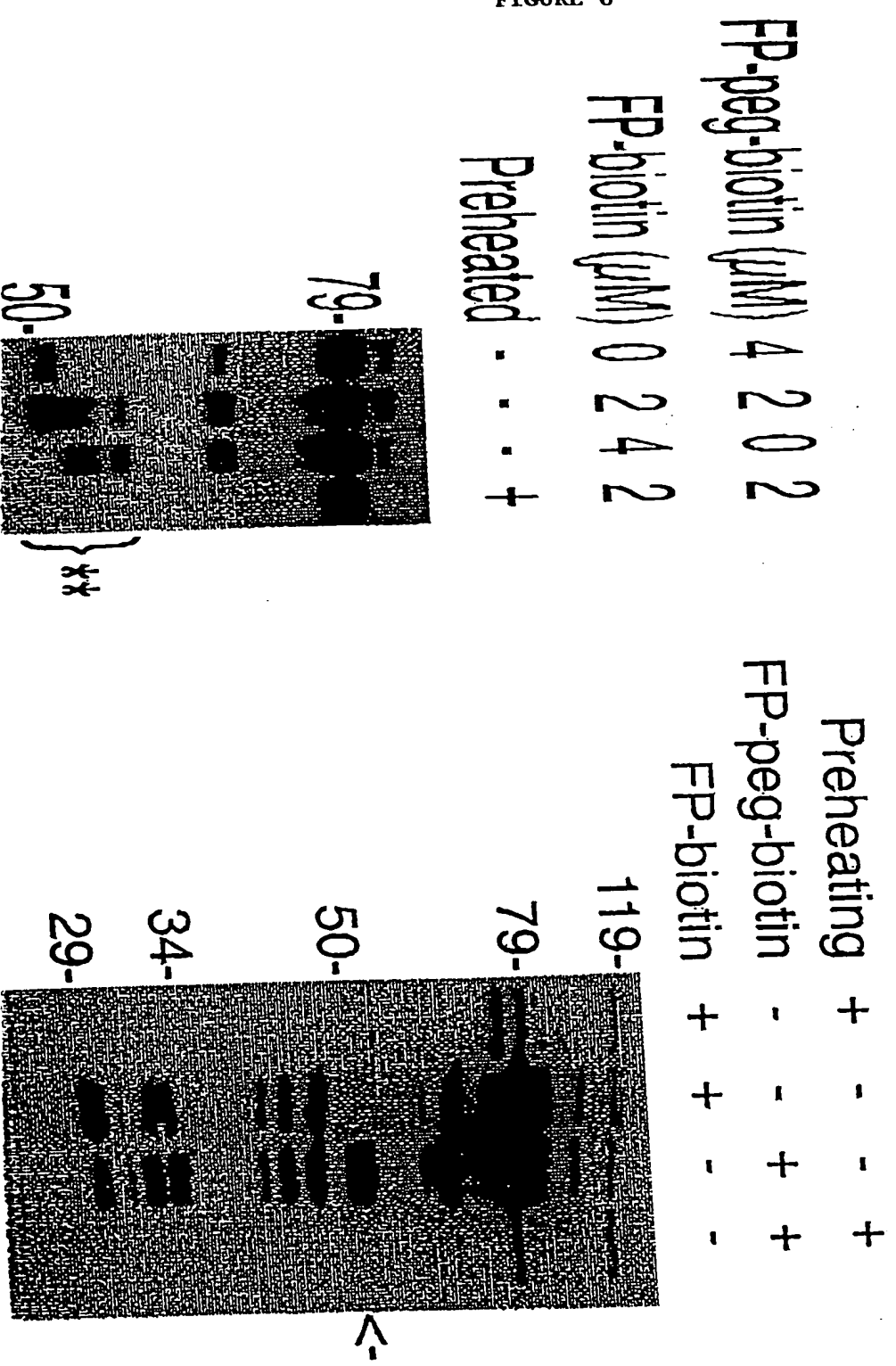
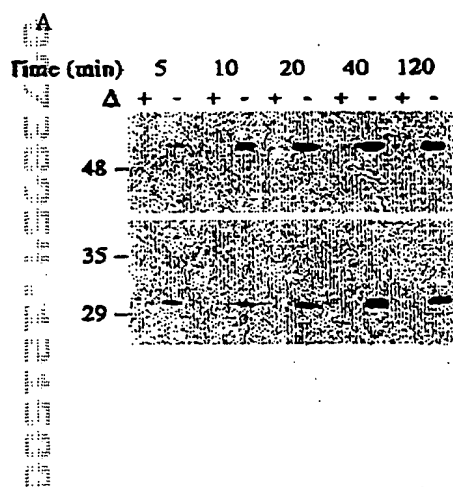


FIGURE 7



B

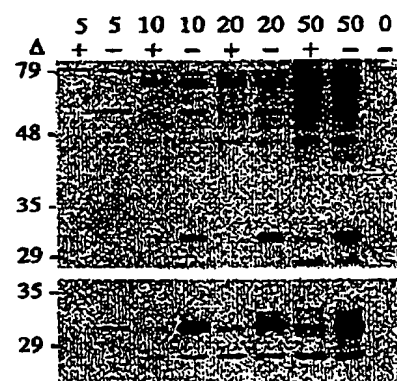
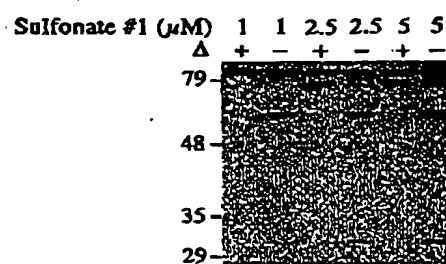
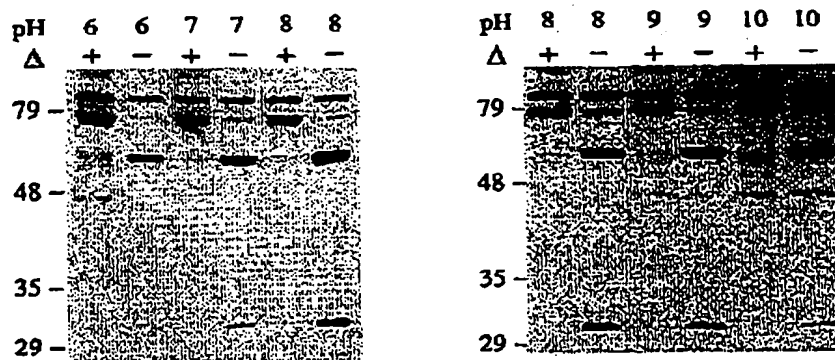
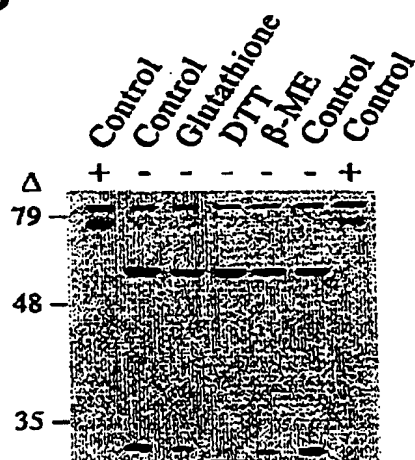


FIGURE 7

C



D



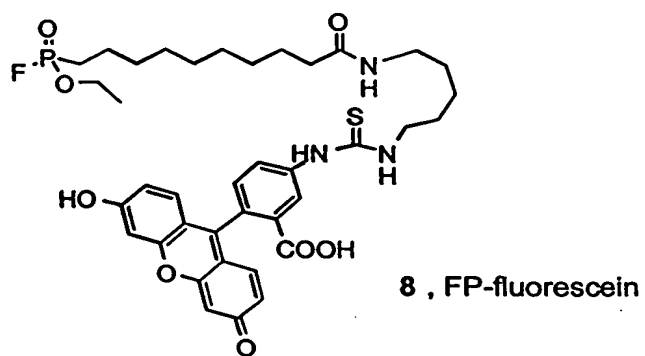
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FIGURE 9

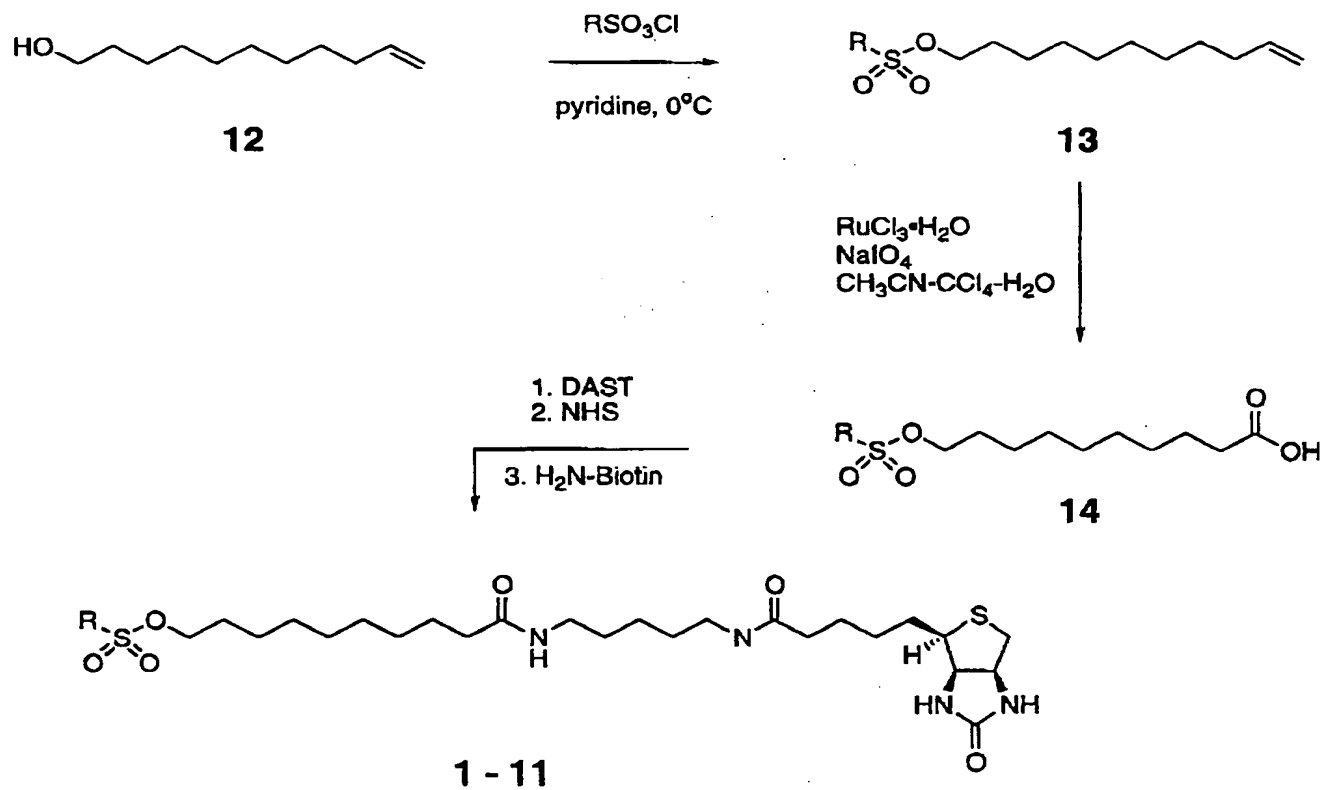
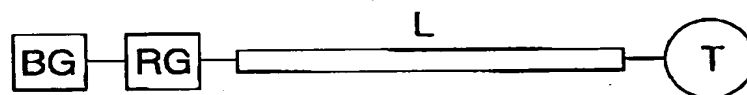


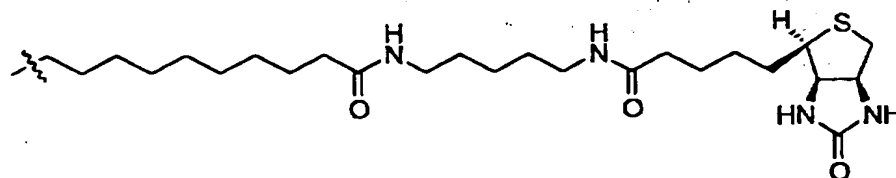
FIGURE 10

A.

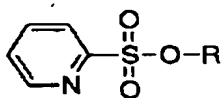


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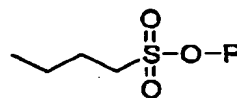
R =



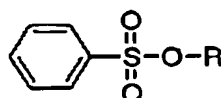
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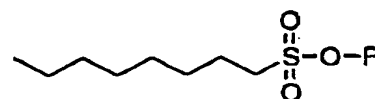
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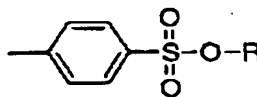
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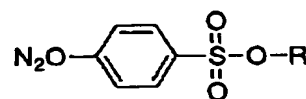
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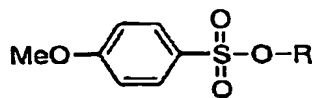
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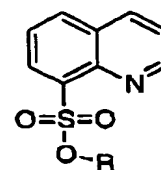
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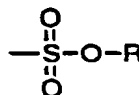
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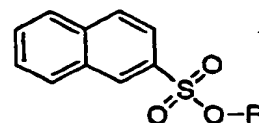
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5



10



11

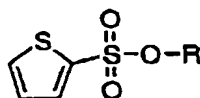
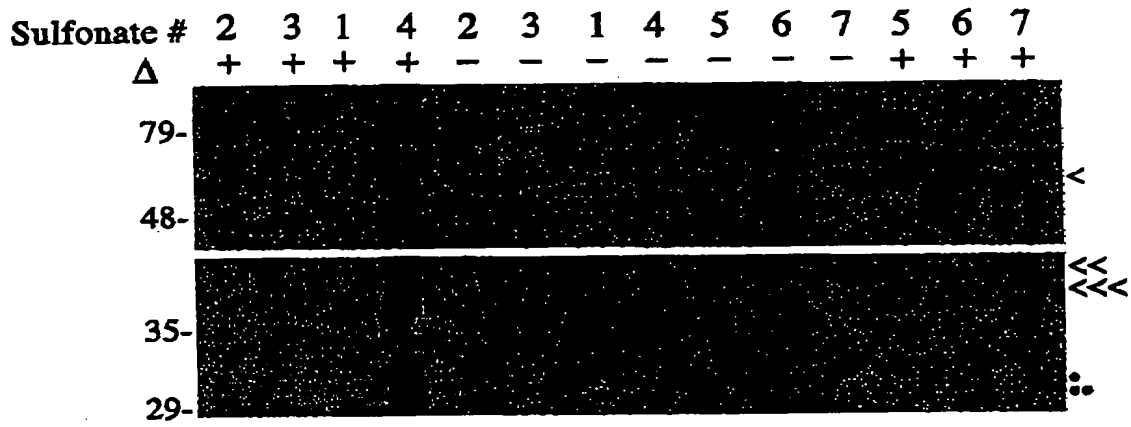


FIGURE 11

A



B

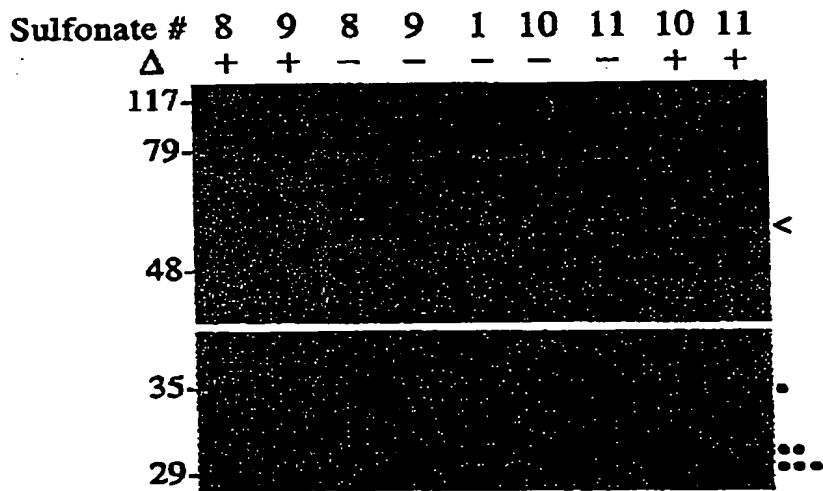
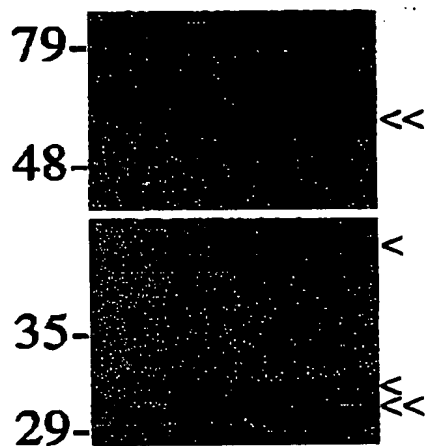


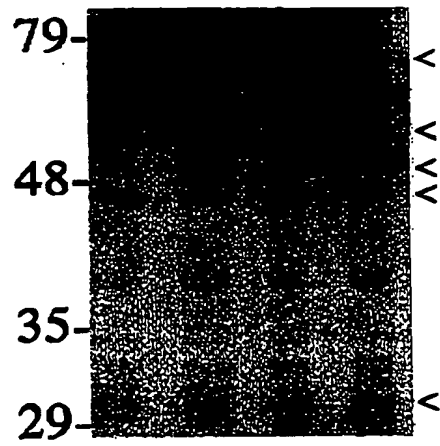
FIGURE 12

A

Sulfonate # 1 1 5 5
 Δ + - - +

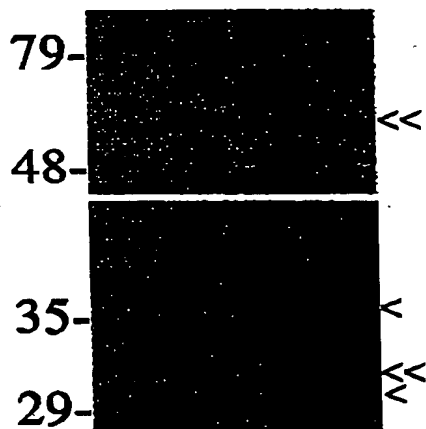


1 1 5 5
+ - - +



B

Sulfonate # 1 1 9 9
 Δ + - - +



1 1 9 9
+ - - +

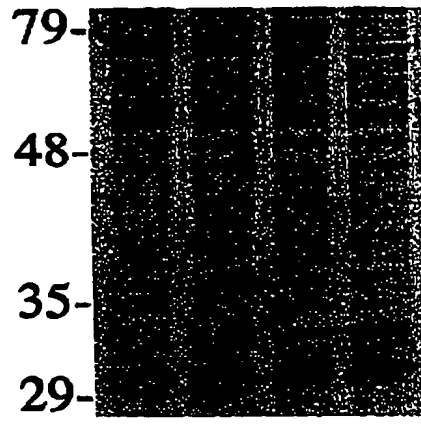
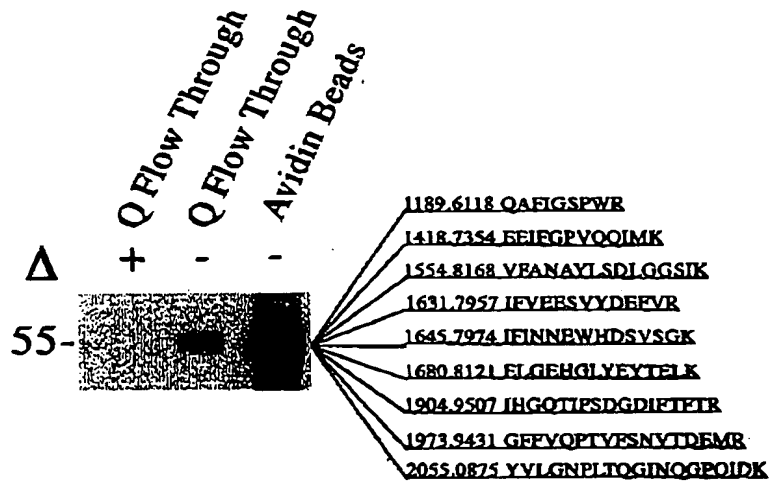
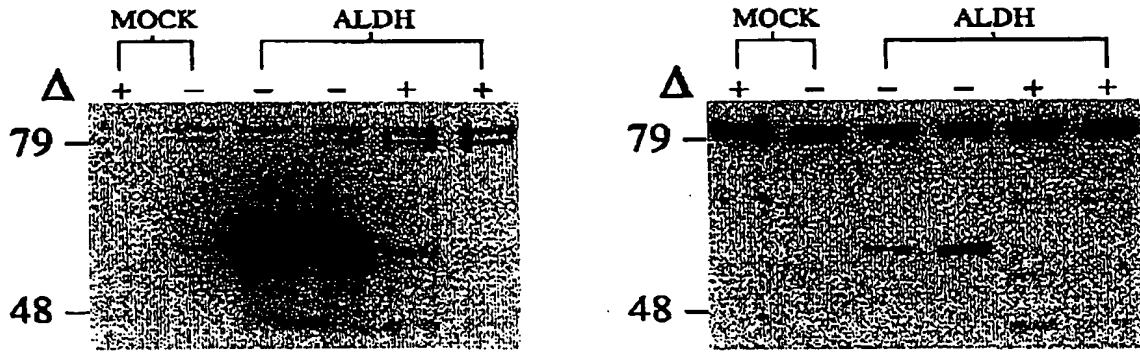


FIGURE 13

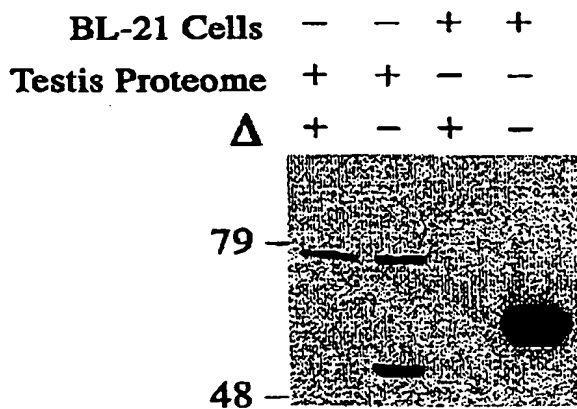
A



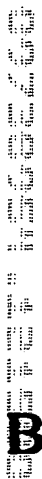
B



C



A



Age Group	Percentage
18-24	79%
25-34	48%
35-44	10%
45-54	10%
55-64	10%
65-74	10%
75-84	10%
85+	10%

FIGURE 15

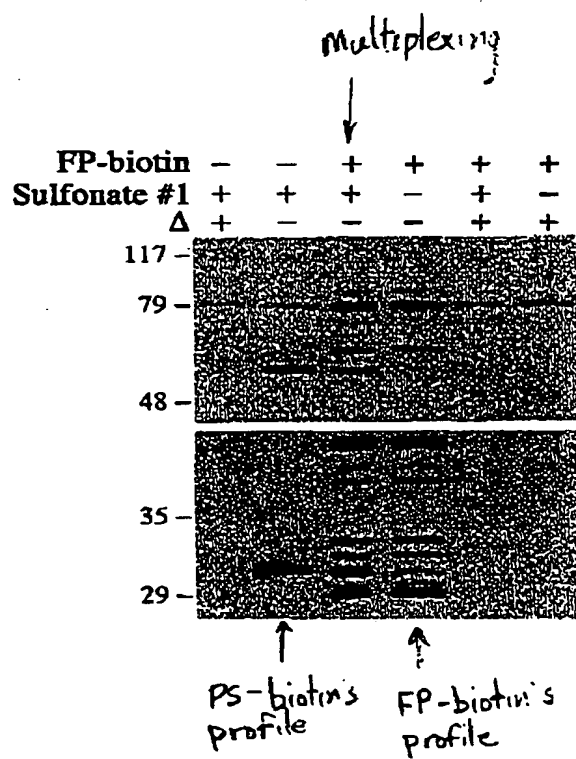


FIGURE 17

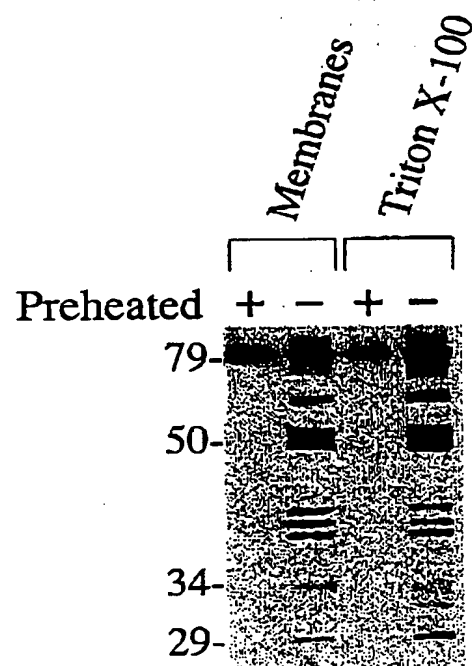


FIGURE 18

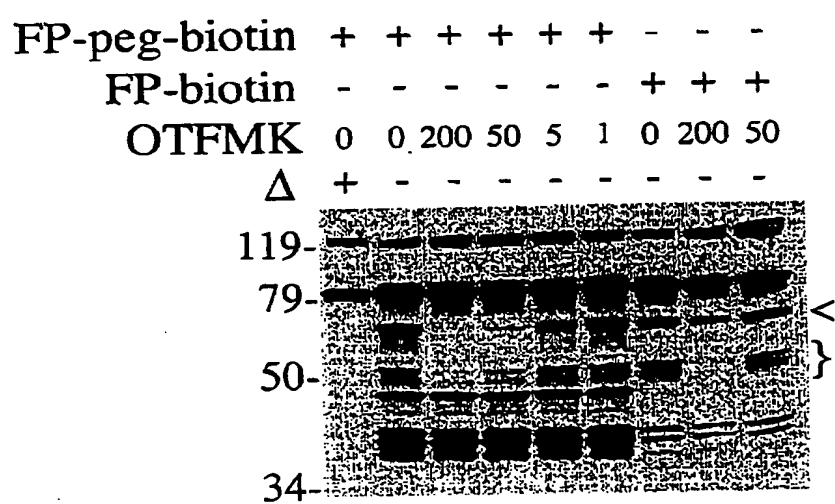


FIGURE 19

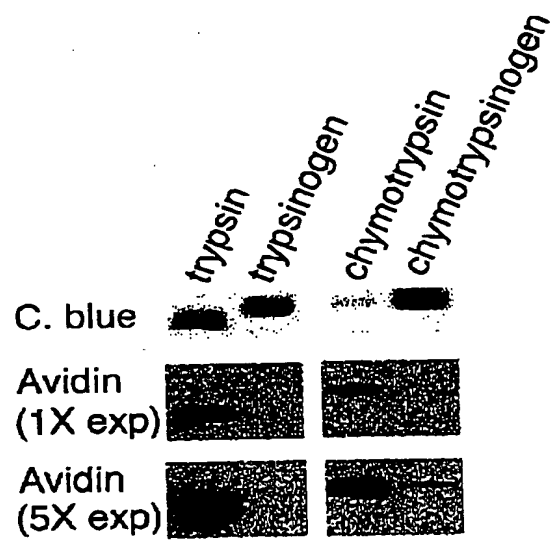
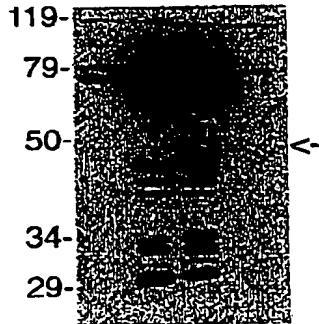


FIGURE 20

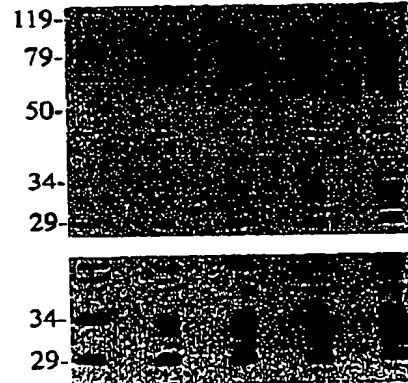
A

FP-peg-biotin	-	-	+	+
FP-biotin	+	+	-	-
Preheated	+	-	-	+



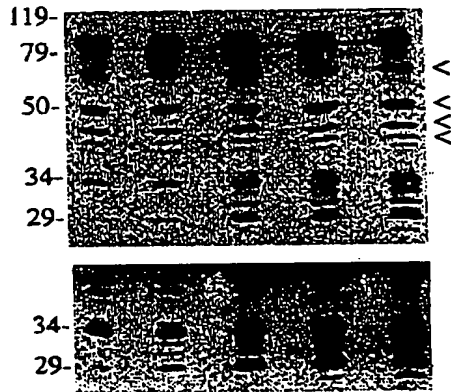
B

FP-biotin (μ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



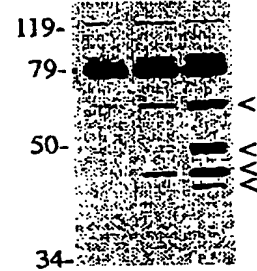
C

FP-peg-biotin (μ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



D

FP-peg-biotin (μ M)	1	2	8
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One minute reaction

FIGURE 21

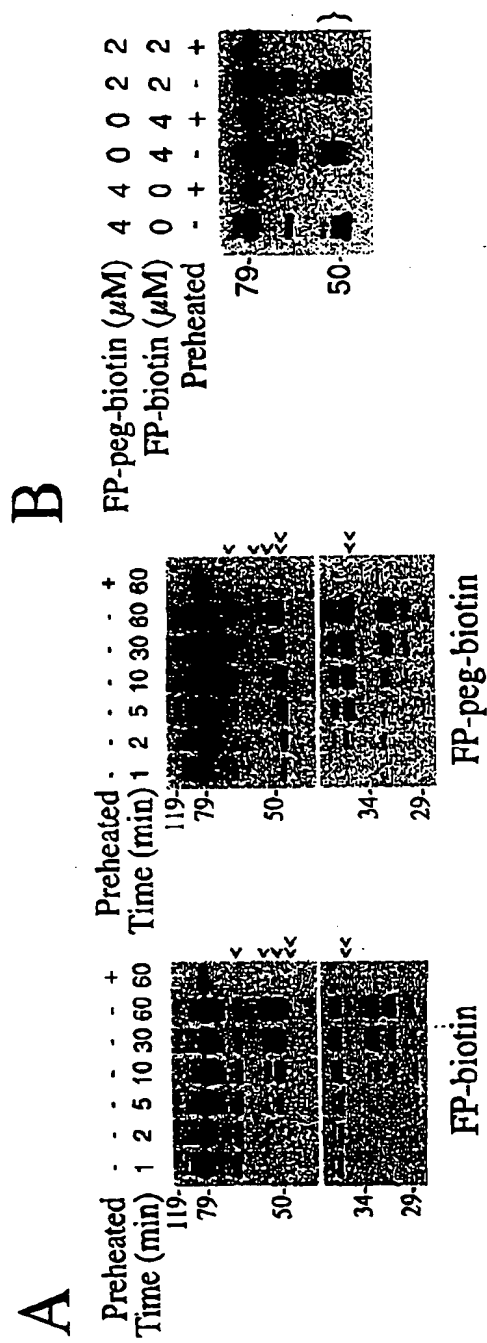


FIGURE 22

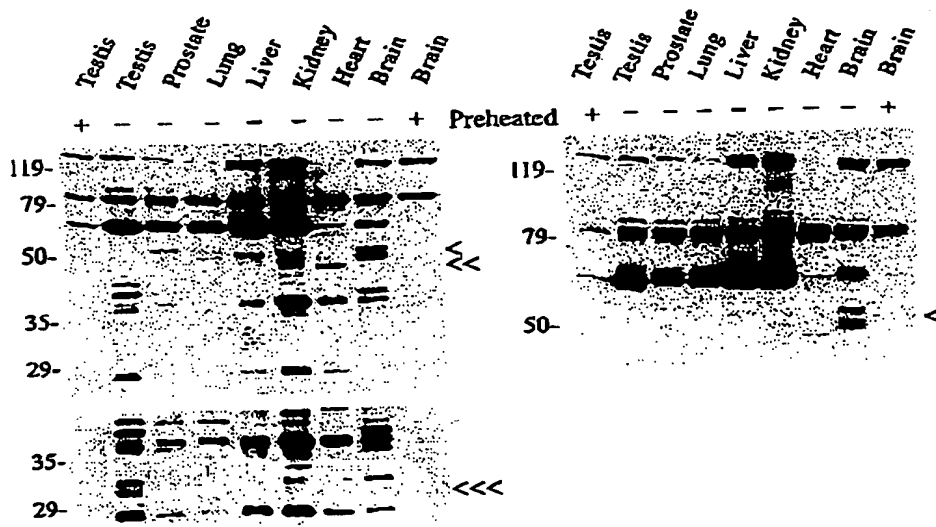


FIGURE 23

